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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,719	09/20/2002	James Robl	103080-P08-058	2839

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ROPES & GRAY LLP
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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

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02/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/070,719	ROBL ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51,52 and 54-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51,52 and 54-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/31/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/07 has been entered.

Applicants' Amendment and Response, filed 10/31/07, has been entered. Claim 51 is amended; claims 56-58 are newly added; claim 53 is cancelled; claims 51, 52, 54-58 are pending and under current examination.

Information Disclosure Statement

Applicants' IDS, filed 10/31/07, has been considered.

Double Patenting

Claims 51, 52, 54-58 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 40-41 of copending Application No. 10/922,374. Applicants argue that they have now amended claim 51 to recite a method of producing a blastula or morula comprising the step of introducing mitochondria or mitochondrial DNA derived from cell(s) of the donor's cells' species. Applicants argue that the '374 application does not reflect the method of the instant claims. These arguments are not persuasive. The claims of the '374 case produce a blastula or morula by insertion of a desired human cell or cell nucleus. Thus, introduction of an entire human cell would encompass introducing mtDNA into the enucleated oocyte.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51, 52, 54-58 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants Arguments. Applicants argue that although they do not provide working examples for the complete method of claim 51, they provide an example of cross-species SCNT (example 1) and a protocol for isolating mitochondria (example 2), and that the specification provides extensive guidance to enable the claimed invention. Applicants argue that because the relative skill of those in the art is extremely high, and additionally in view of the guidance of the specification, the specification enables the claimed invention. See pages 5-6 of the Response.

Applicants argue that although there is a low-efficiency in producing interspecies NT units, this does not evince unpredictability or undermine enablement, because the experimentation would not be undue. Applicants argue that the methods taught by the instant application are predictable and reproducible, as evidenced by Chang *et al.*, because Chang show cross-species NT by inserting human somatic nuclei into bovine oocytes, using the same methods as instantly-filed disclosure, therefore, Applicants argue, Chang supports Applicants' contention that the claimed invention is enabled. See pages 6-7 of the Response.

Response To Arguments. These arguments are considered, but are not persuasive. The claims are specifically directed to methods of producing blastula or

morula. The Examiner responds that that the standard, under 112, 1st paragraph is to teach the skilled artisan how to make and use the claimed invention. Applicants elected a method of producing embryonic or stem-like cells produced by their claimed methods. Although the claims have been amended to recite the production of a morula or blastula, there is no other enabled use that is contemplated by the specification within Applicants' election, other than to produce embryonic or stem-like cells. That is, even if one of skill in the art were able to produce morula or blastula stage embryos utilizing Applicants' methods, one of skill in the art would have to practice undue experimentation to use the claimed invention for its contemplated purpose, within Applicants' elected invention, which is to produce embryonic or stem-like cells. Additionally, given that only one NT unit was produced, and no ES cells were produced from this NT unit, one of skill in the art could not rely upon the state of the art of producing ES cells to enable the claimed invention. There is no other use that is enabled for producing a morula or blastula embryo in the context of Applicants' invention; therefore, the rejection of record is maintained. See also, Roach & McNeish and Thomson with regard to the unpredictability in the art of producing embryonic stem cells.

Furthermore, with regard to the Chang reference, the Examiner responds that although Chang teach the production of blastocyst stage embryos, many of the blastocysts had abnormal number of chromosomes, and even in light of the production of normal embryos, it is clear that Chang *et al.* show that cross-species NT is an unpredictable process. If one were to use the blastocysts to produce ES cells (as contemplated in the specification), using a blastocyst with an abnormal karyotype would result in an ES cell with abnormal karyotypes. This is not within the definition of an ES cell. For example, Pera (J. of Cell Science, 113: 5-10, 2000) teaches that ES cells must originate from a pluripotent cell population, maintain a normal karyotype, can be propagated indefinitely, and are capable of spontaneously differentiation into cells of all three embryonic germ layers in teratomas or *in vitro*

(see p. 6, col. 2). Additionally, ES cells must have specific, art-recognized markers (such as SSE—3, SEA-4, TRA-1-60, TRA-1-81, Alkaline phosphatase and Oct-4). See NIH (Chapter 3, *Stem Cells: Scientific Progress and Future Research Directions.* Department of Health and Human Services. June 2001. http://stemcells.nih.gov/info/scireport/2001report). There is no specific guidance provided by the specification or art of record, with regard to isolating embryonic or stem-like cells from morula or blastula that fulfill the art-recognized characteristics and definition of ES cells.

The Examiner maintains that the specification generally teaches the claimed method steps, but does not provide an enabling disclosure for the claimed invention. In particular, in light of the lack of an enabled use for the morula or blastula stage embryo produced by the claimed methods, as well as the unpredictability in the art with regard to the production of abnormal blastocysts in cross-species nuclear transfer, the lack of working examples provided, it would have required undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Applicants' Arguments. Applicants argue that the benefits of introducing mtDNA do not necessarily require incorporation of the DNA into the oocyte. Even if long term stability of donor-derived mtDNA is in doubt in a particular species, Chang provides guidance to show that the short term stability of donor-derived mtDNA is undisputed, and that it is apparent from the prior art in the field that incompatibility with the nucleus with mitochondria during interspecies SCNT completes cloning, and thus, that supplementing SCNT procedures may be useful for improving cloning methods. Applicants conclude that the claimed invention is enabled for its breadth because the post-filing art supports their invention, and that the tools available to the skilled artisans permitted the practice of the claimed invention without undue experimentation. See pages 8-10 of the Response.

Response to Arguments. These arguments are not persuasive. This is not persuasive. The arguments of counsel cannot take the place of evidence in the record. See *In re* Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965) and MPEP §716.01. Applicants have not provided an appropriate affidavit or declaration supporting that supplementing SCNT procedures improves cloning methods. The Examiner asserts that the prior art of record clearly shows that cross-species nuclear transfer is unpredictable (see Wolfe, Gurdon, Meirelles, Dominko, Dominko (1999)), and further, that the introduction of mtDNA is unpredictable with regard to the further development of the NT unit (see Jiang and Chen). Thus, these unpredictibilities, coupled with the lack of an enabled use of the morula or blastula stage NT unit, fail to enable the claimed invention. The post-filing art of Mastromonaco *et al.* show that even between close species, cross-species SCNT is highly unpredictable, see p. 4, 1st full ¶.

Applicants point to p. 14, lines 9-11 for support to show that the cells produced by the methods may be used to study differentiation and for assay purposes. See p. 7 of the Response. The Examiner responds that although this citation discusses using the cells for differentiation studies or assay purposes, this citation requires the embryonic or stem-like cells, not the actual morula or blastula NT unit as claimed. It is reiterated that the skilled artisan, given the teachings of the specification, would clearly understand that the cells of the invention are embryonic or ES-like cells and would therefore have ES cell properties.

The specification is not enabling for the breadth of the claimed invention. The specification fails to overcome the above-recited unpredictibilities in cross-species nuclear transfer, the unpredictability in maintenance of the donor mtDNA, the importance of mtDNA in embryonic development, as well as in the production of embryonic or ES-like cells. One of skill in the art would not be able to practice the claimed invention, as broadly claimed, because the specification fails to provide guidance to practice the claimed invention, and the art provides significant

teachings of the unpredictability found in the art, with regard to cross-species NT, and producing ES cells from the resultant NT unit. Because the intended use of the claimed method is to produce embryonic stem cells, one of skill in the art would recognize that the NT unit would need to be able to develop to blastocyst stage, with the expression of appropriate markers and karyotype, in order to produce ES cells. The specification provides no other enabled use for the morula or blastula, produced by the NT method, within the context of Applicants' claimed invention. Accordingly, it is maintained that it would have required undue experimentation for one of ordinary skill in the art to practice the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Peter Paras, SPE of Art Unit 1632, at (571) 272-4517. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Thaian N. Ton/
Primary Examiner
Art Unit 1632